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Food and Drug Administration
Center for Devices and Radiological Health
Regulations Staff (HFZ-215)
1350 Piccard Drive
Rockville, MD 20850

RE: 513(f) Reclassification Petition for PTCA Balloon Catheters (74LOX)

Dear Sir/Madam:

The enclosed information is submitted for the agency's consideration in downclassifying PTCA balloon catheters from Class III to Class II. Due to the extensive use of these devices in interventional cardiology techniques for nearly twenty years, there is an abundant amount of information available. Included in the enclosed reclassification petition is a summary of this information, describing the well known risks associated with device use and recommendations for minimizing their occurrence. This summary provides valid scientific evidence supporting downclassification of the device. Please review this petition for the PTCA balloon catheters and notify me if anything further is needed.

Thank you for the opportunity to submit this information.

Sincerely,

Neal E. Fearnot

Neal E. Fearnot, Ph.D.
President

Enclosures

NEF:mlb

OOP-1533

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# *513(f) RECLASSIFICATION PETITION FOR PTCA BALLOON CATHETERS*

## *SUPPLEMENTAL DATA*

## I. DESCRIPTION OF PERCUTANEOUS TRANSLUMINAL CORONARY ANGIOPLASTY BALLOON CATHETER

The percutaneous transluminal coronary angioplasty (PTCA) balloon catheter is indicated for balloon dilatation of a hemodynamically significant coronary artery or bypass graft stenosis in patients evidencing coronary ischemia for the purpose of improving myocardial perfusion. The PTCA balloon catheter has a single or double lumen shaft with a balloon near the distal tip. The catheter typically features a minimally compliant balloon constructed from a high density polymer. The balloon is designed to uniformly expand to a specified diameter and length at a specific pressure as labeled, with acceptable rates of inflation and deflation and acceptable burst pressure. The device generally features a type of radiographic marker to facilitate fluoroscopic visualization of the balloon during use. This device is used in conjunction with other conventional PTCA equipment, including, but not limited to, a vascular access set, arterial sheath, guiding catheter, guide wire, indeflator, and contrast mediums.

## II. RISKS TO HEALTH POSED BY PERCUTANEOUS TRANSLUMINAL CORONARY ANGIOPLASTY BALLOON CATHETERS

The long history of use of PTCA balloon catheters and the large number of published clinical reports show that the potential risks related to this type of device are well known and extensively documented. Table I summarizes these associated risks, typical causes, and corresponding recommendations for minimizing their occurrence. Information regarding these potential risks and associated recommendations may be incorporated in labeling guidance for PTCA balloon catheters to serve as a special control.

The information summarized in Table I is based on scientific publications covering a span of over 18 years of clinical use of PTCA balloon catheters (72 articles dating from 1982 to 2000). Please refer to Section VI of this submission for text summarizing this information.

## TABLE I: SUMMARY OF POTENTIAL RISKS OF PTCA BALLOON CATHETERS

| PROBLEM | CAUSE | COMMENT | REF. |
|---|---|---|---|
| Acute vessel closure | • Thrombus<br>• Coronary artery dissection<br>• Coronary artery spasm | • Use inflated balloon diameter approximating vessel diameter proximal and distal to the stenosis<br>• Use appropriate anticoagulant, antiplatelet and coronary vasodilator therapy<br>• Manipulate catheter only under high-quality fluoroscopy | 2, 8, 18, 20, 24 |
| Coronary artery dissection, perforation, rupture | • Due to expansion of intramural hematoma<br>• Balloon rupture<br>• Balloon too large for vessel<br>• Perforation or rupture of vessel with guide wire or catheter by use of excessive force while advancing | • Use appropriate size balloon catheter<br>• Do not exceed balloon's rated burst pressure<br>• Advance the guide wire and catheter carefully<br>• Manage with prolonged balloon inflation, stents, embolization of vessel, or CABG | 5, 10, 12, 13, 15, 31, 37, 63 |
| Acute MI and unstable angina | • Failure of procedure<br>• Thrombus<br>• Vessel spasm<br>• Vessel dissection | • Use careful operative technique<br>• Use care in patient selection<br>• Monitor patient closely<br>• Fractionate expansion time based on S-T segment on ECG | 5, 14, 22, 62 |
| Coronary artery spasm | • Endothelial dysfunction and spontaneous increase in coronary vasomotor tone in presence of atherosclerotic plaque<br>• Tobacco and cocaine abuse increase susceptibility | • Obtain patient history regarding susceptibility<br>• Consider use of vasodilators<br>• Monitor patient closely | 55 |
| Arrhythmias | • Myocardial ischemia<br>• Hypoxemia<br>• Stimulation of myocardium with guide wires or catheters<br>• Vagal stimulation<br>• ICD | • Avoid unnecessary stimulation of the myocardium and coronary vessels with the guide wire or catheter<br>• Fractionate inflation time to manage ischemia during inflation<br>• Anticipate pharmacological or other intervention (*e.g.*, pacemaker) | 52, 60 |

| PROBLEM | CAUSE | COMMENT | REF. |
|---|---|---|---|
| Embolization or fragmentation of thrombotic or atherosclerotic material | • Fracture of plaque | • Place stent following angioplasty<br>• Aspirate embolized thrombus | 30, 64, 65 |
| Air embolism | • Incomplete aspiration of guiding catheter<br>• Balloon rupture<br>• Insinuation of air with balloon catheter introduction or withdrawal<br>• Structural failure of the equipment | • Aspirate air bubbles through the guiding catheter<br>• Use only the recommended balloon inflation medium (no air or gaseous medium)<br>• Pre-flush catheter lumens and purge air from indeflator<br>• Use meticulous technique | 4, 33, 49, 50 |
| Hypo/hypertension | • Bleeding<br>• Medication related<br>• Pain<br>• Inadequate peripheral perfusion | • Use close hemodynamic monitoring<br>• Use adequate sedation and pain control<br>• Administer vasodilators properly<br>• Avoid extremes in blood pressure | 62 |
| Stroke | • Air embolus<br>• Embolus of thrombus or atherosclerotic material<br>• Hypertension<br>• Hypotension | • Use careful interventional technique<br>• Monitor carefully for emboli<br>• Treat hypertension during PTCA to minimize occurrence of hemorrhagic stroke<br>• Avoid hypotension | 33 |
| Reaction to contrast agent | • Contrast allergy<br>• Contrast agent nephropathy<br>• Renal insufficiency<br>• Beta blockers | • Obtain thorough medical history<br>• Use non-ionic contrast in high risk patient<br>• Use proper IV hydration<br>• Minimize volume of contrast agent | 56, 57 |
| Coagulopathy | • Excessive heparinization<br>• Use of the newer and more potent antithrombotic agents | • Use close clinical and laboratory monitoring<br>• Control using medication | 62 |
| Aneurysm formation | • Damage to coronary vessel wall with subsequent aneurysmal dilatation | • Use careful interventional technique | 68, 69, 70 |

| PROBLEM | CAUSE | COMMENT | REF. |
|---|---|---|---|
| Vascular access site complications<br>• Hematoma<br>• A-V fistula<br>• Infection<br>• Pseudoaneurysm | • Use of excessive force<br>• Difficult device placement<br>• Inadequate pressure placed on access site after procedure<br>• Simultaneous puncture of adjacent artery and vein<br>• Inadequate aseptic technique<br>• Decreased host defenses | • Use meticulous interventional and sterile technique<br>• Use adequate pressure on site after procedure<br>• Monitor with color doppler imaging<br>• Use vascular sealing device<br>• Place stent | 6, 11, 17, 46,66, 71 |
| Restenosis | • Fibrocellular proliferation at the site of PTCA in the vessel wall<br>• Inadequate dilatation of the artery by PTCA | • Use stenting after angioplasty<br>• Use adequate balloon dilatation of the coronary vesel | 21, 23, 25,72 |
| Emergency bypass surgery | • Failure of angioplasty<br>• Coronary dissection<br>• Coronary occlusion | • Use meticulous interventional technique<br>• Use care in patient selection | 5, 14, 22, 28, 32, 34, 42, 45, 62 |
| Death | • Bleeding complications<br>• Acute MI<br>• Failured procedure<br>• Arrhythmia<br>• Emergency bypass | • Use careful operative technique<br>• Promptly intervene in case of complications<br>• Monitor patient closely<br>• Anticipate need for surgical intervention, with surgical team on alert | 3, 5, 8, 14, 20, 53, 54, 67 |
| Balloon rupture | • Over-pressurization of balloon<br>• Defective balloon<br>• Calcification<br>• Use of inappropriate balloon inflation medium | • Use pressure monitor device to prevent over-pressurization | 5 |
| Guide wire fracture or entrapment | • Excessive tortuousity | • Use caution in patients with complex anatomy | 26, 58, 59 |
| Failed procedure | • Inability to cross lesion<br>• Inability to expand lesion<br>• Inadequate balloon pressure<br>• Balloon rupture | • Perform PTCA only by properly trained physicians<br>• Have experienced physician standing by to assist inexperienced operator | 9, 19, 29, 40, 41, 62 |

## III. SPECIAL CONTROLS TO ADDRESS DESCRIBED RISKS

Special controls within the meaning of section 513(a)(1)(B) of the Act may include guidance documents, labeling, design validation testing, postmarket surveillance, or any mechanism that could provide a reasonable assurance of safety and effectiveness. The Food and Drug Administration has not established special controls for PTCA balloon catheters. However, given the significant accumulated experience, sufficient information exists to establish special controls to support reasonable assurance of safety and effectiveness.

Use of PTCA balloon catheters is viewed as safe when performed by cardiologists experienced in interventional techniques, and have proven to be a useful adjunct to surgery and medical management. The associated potential problems, low complication rates, and overall performance assessments over the last 20 years as described in numerous scientific journal articles show PTCA balloon catheters to offer reasonable assurance of safety and effectiveness for their intended use.

Several guidance documents have been issued by the FDA to provide assurance that design and construction of PTCA balloon catheters are suitable for their intended use and to address labeling requirements. These documents include: *Guidance for the Submission of Research and Marketing Applications for Interventional Cardiology Devices: PTCA Catheters, Atherectomy Catheters, Lasers, Intravascular Stents* (May 1994), and *Percutaneous Transluminal Coronary Angioplasty Package Insert Template* (February 7, 1995). Please refer to Table I for suggested information and clinical considerations to incorporate into the existing labeling guidance, which already includes a number of these recommendations. These guidance documents may serve as special controls to provide reasonable assurance of safety and effectiveness of use of PTCA balloon catheters, and provide support in managing risks which are not otherwise addressed by general controls alone.

In addition to the proposed special controls of device testing and labeling guidances, there are existing control mechanisms in place to track device performance against an established baseline. The mandatory Medical Device Reporting system (MDR/MAUDE databases) is an established mechanism for tracking adverse device

outcomes, containing information dating back to 1985 for PTCA balloon catheters. Another established mechanism providing baseline device performance information is the FDAMA (1997) provision, which allows the agency to use information from preclinical and clinical studies of PMAs six years after approval. This information may be used in premarket review to establish a performance standard or special control, or for device classification/reclassification.

In summary, with the Food and Drug Administration using device testing and labeling guidance as established special controls, ensuring compliance with general controls (such as adherence to Good Manufacturing Practices), and having established baseline information on device performance through the MDR/MAUDE reporting systems and through available PMAs, the safety and effectiveness of these devices may be reasonably assured, warranting reclassification of PTCA balloon catheters into Class II.

## IV. POTENTIAL BENEFITS OF PTCA BALLOON CATHETERS

Benefits of PTCA balloon catheters include minimally-invasive methods of treating coronary artery stenosis. The balloon is inserted percutaneously and the deflated balloon is advanced into the narrowed part of the coronary artery. Balloon angioplasty is performed by inflating the balloon, compressing the plaque, and enlarging the inner diameter of the blood vessel so that blood can flow more easily. Use of a PTCA balloon is a less traumatic and less expensive alternative to bypass surgery for some patients with coronary artery disease, and is often used in combination with stent placement (representing 70 to 90% of procedures).

Based on the long history of use of PTCA balloon catheters, the considerable experience that has been gained, and the extensive clinical information that has been published, PTCA balloon catheters are viewed as safe and effective treatment for the management of patients with coronary artery or bypass graft stenosis. With careful attention to technique by experienced personnel, complications associated with use of these devices can be minimized.

## V. RECOMMENDATIONS FOR CLASS

Based on the extensive information published over the last two decades related to clinical experience of PTCA balloon catheters and the number of PMA applications that have been approved since 1979 for this device type, general and special controls are available, or may be established, to reasonably assure their safe and effective use. Required testing for PTCA balloon catheters is outlined in the *Guidance for the Submission of Research and Marketing Applications for Interventional Cardiology Devices*, May 1994 and may serve as a special control. Specific device labeling, incorporating information pertaining to potential complications with recommendations for their minimization, may also serve as a special control. Compliance and adherence to the Quality Systems Regulation and Good Manufacturing Practices and use of the MDR/MAUDE reporting systems may serve as general controls. With these general and special controls available to provide reasonable assurance of safety and effectiveness, it is hereby recommended that PTCA balloon catheters, product code 74LOX, be reclassified into Class II.

## VI. SUMMARY OF VALID SCIENTIFIC EVIDENCE SUPPORTING RECOMMENDATION

Since the 1980's, a great deal of clinical experience has been reported on PTCA balloon catheters. The balloon catheters are inserted percutaneously by interventional cardiologists to expand stenosed coronary arteries, with or without the placement of a stent. Initially, because experience was limited, the coronary angioplasty technique was disseminated informally among physicians who were highly experienced at diagnostic cardiac catheterization. As the coronary angioplasty knowledge base grew and techniques evolved, standards were developed for training cardiologists. Formal angioplasty training programs were first organized in the early 1980's. Proposals for training standards were first published in 1986. The most recent recommendations were published by the American College of Cardiology in 1995. Along with the growing expertise of physicians performing these procedures, the balloon catheters themselves have been

modified and improved, and the stenotic lesions and patients judged to be appropriate for PTCA has expanded.[16, 27, 35, 36, 38, 39, 43, 44, 48, 55, 61]

Because of the long historical experience of PTCA balloon catheters and the large number of clinical publications, the information available is extensive. There are well-controlled investigations, partially-controlled studies, studies and objective trials without matched controls, well-documented case histories conducted by qualified experts, and reports of significant experience with a marketed device. Records to date indicate that since 1979 at least 19 PMA applications have been approved for this device type (product code 74LOX). The feasibility and efficacy for use of these PTCA balloon catheters are shown in their long history of use and the successful clinical results. The following text summarizes the potential associated risks which have been noted in Table I (Section II of this submission) with recommendations for minimizing their occurrence. From this information it can be fairly and reasonably concluded by qualified experts that there is reasonable assurance of the safety and effectiveness of this device under its conditions of use.

Coronary angioplasty produces a controlled vascular injury, fracturing plaque in the coronary artery in order to expand the vessel and increase blood flow. However, the treated site's response to this intervention may not result in a stable patent result. A commonly reported occurrence is acute vessel closure due to thrombus formation, coronary artery dissection or spasm.[2, 8, 18, 20, 24] Although in some instances it may not be possible to determine the etiology of the acute vessel closure, there are recommendations to follow. Before insertion of the catheter, appropriate anticoagulant, antiplatelet, and coronary vasodilator therapy should be administered. While in the vascular system, the catheter should be manipulated while under high-quality fluoroscopic observation. To minimize the occurrence of vessel injury, it is important that the inflated diameter of the balloon approximate the diameter of the vessel just proximal and distal to the stenosis.

Another risk known to be associated with angioplasty is injury to the coronary vessel wall, resulting in dissection, perforation, or rupture.[5, 10, 12, 13, 15, 31, 37, 63] A mild injury to the vessel wall may be self-limited and cause no adverse event for the patient, or the injury may be extensive and cause catastrophic complications. Vessel injury can be due

to a number of factors: balloon rupture, perforation or rupture of the vessel with a guide wire or catheter, using a balloon which is too large for the vessel, and expansion of an intramural hematoma. To avoid balloon rupture, it is important not to exceed the balloon's rated burst pressure. Advancing the guide wire or catheter carefully by avoiding excessive force will help to decrease the occurrence of perforation. Again, it is important to use a correctly sized balloon catheter for the targeted lesion. Although coronary perforations have been managed with prolonged balloon inflations, stents, or embolization of the vessel,[63] thoracotomy may be necessary to repair the damaged vessel.

Acute myocardial infarction (MI) and unstable angina are a known complication of angioplasty, and should be considered when intervening in patients with compromised myocardial perfusion. Causes of MI or angina may include failed angioplasty, thrombus formation, vessel spasm or vessel dissection.[5, 14, 22] The definition of periprocedural MI has been somewhat problematic, in contrast to other major cardiac complications such as death or emergency bypass surgery which are easily recognized. Some definitions of myocardial infarction require the development of Q waves in addition to a threshold value for enzyme elevations. However, more recent reports have identified non-Q wave MI's with enzyme elevations three to five times the upper limit of normal as having clinical significance. The current recommendation is that the complication rate from Q-wave MI be less than 1.5%. Careful patient selection should help to decrease this complication. It has been recommended to fractionate the balloon expansion time based on the S-T segment of the ECG. Angioplasty is contraindicated, in general, in patients with left main coronary disease who are candidates for coronary bypass and asymptomatic patients with critical stenoses in relatively unimportant coronary arteries or with noncritical stenoses.[62]

Coronary artery spasm is caused by endothelial dysfunction in the presence of atherosclerotic plaque, and is therefore a risk during angioplasty. Patients with coronary atherosclerosis may have spontaneous increases in coronary vasomotor tone, resulting in myocardial ischemia. Tobacco and cocaine abuse are important risk factors for the provocation of vasospasm.[55] It is therefore important to obtain a thorough patient history to determine susceptibility to this complication. The use of vasodilators should be considered.

Arrhythmias are a fairly frequent complication of angioplasty, and coronary interventional procedures in general.[60] Patients with heart disease have a rate of arrhythmias higher than the general population. Etiologies of conduction disturbances in the setting of angioplasty include hypoxemia, stimulation of myocardium with guide wires and catheters, vagal stimulation, and myocardial ischemia. Spurious detection of ventricular fibrillation during PTCA by a transvenous implantable cardioverter defibrillator (ICD) has also been reported.[52] Some of the common conduction disturbances include bradycardia, tachycardia, atrial fibrillation, ventricular fibrillation, and ventricular tachycardia. To minimize the occurrence of arrhythmias, unnecessary stimulation of the myocardium and coronary vessels with the guide wire and catheter should be avoided. It is also important to fractionate the balloon inflation time to manage ischemia during inflation. Appropriate use of antiarrhythmics can treat certain conduction disturbances seen during PTCA. Depending on the type and severity of the arrhythmia, other interventions such as a pacemaker may be necessary.

Embolization or fragmentation of thrombotic or atherosclerotic material may result when plaque is fractured at the time of balloon inflation during angioplasty.[30] Some embolization of fragments would be expected, however the clinical outcome to the patient is dependent on the size of the fragments embolized. Distal embolization is reported as a frequent complication of angioplasty of diseased saphenous vein grafts.[64] Multiple tiny fragments may have no significant consequence, but one large fragment could cause significant occlusion of a vessel. To minimize the risk of embolization, stenting may be performed. Aspiration of embolized thrombus through the guiding catheter has also been reported.[65]

Air embolism, another reported complication during angioplasty, can be a result of incomplete aspiration of guiding catheters, balloon rupture, insinuation of air with balloon catheter introduction or withdrawal, or structural failures of the equipment. [4, 33, 50] Symptomatic responses in the patient can range from mild angina to full cardiac arrest. Because symptoms tend to resolve spontaneously within five to ten minutes, treatment is aimed at supporting the patient for this brief period. Aspiration through the guiding catheter to remove the air bubbles has been recommended.[49] The occurrence of air

embolism can be decreased by careful attention to technique, pre-flushing catheter lumens and purging air from the indeflator, thorough filling of guiding catheters, and using only the recommended balloon inflation medium (never air or any gaseous medium).

Hypotension and hypertension are not uncommon during PTCA due to pre-existing heart and vascular disease in this patient population. Patients are commonly on antihypertensives and other medications at the time of their procedure. Combined with the various medications and interventions used at the time of angioplasty, some variability in blood pressure can be expected. Differing susceptibilities of patients to extremes in blood pressure will govern the long-term consequences of such fluctuations. Hypotension can be caused by bleeding complications, medications, or as a result of inadequate peripheral perfusion due to left ventricular failure. Using adequate sedation and pain control, and appropriate administration of vasodilators may minimize blood pressure extremes during the procedure. Careful hemodynamic monitoring can detect worrisome trends in blood pressure, which can be addressed by the cardiologist, skilled in such interventions.

Stroke, a risk of the angioplasty procedure, can be caused by embolization of thrombus, atherosclerotic material, or air. Extremes of blood pressure combined with anticoagulation during interventional procedures can also be an etiology of stroke.[33] When the PTCA balloon catheter is inflated, the atherosclerotic plaque is ruptured, and fragments may embolize. Fragments of thrombus or air bubbles may also be a source of embolic material, lodging in a central nervous system vessel and causing a transient ischemic attack or stroke. Sustained hypotension during the procedure leading to underperfusion can cause a permanent neurologic deficit in a susceptible individual, and uncontrolled or poorly controlled hypertension can be an etiology for hemorrhagic stroke. Steps can be taken to minimize or prevent embolism of air, thrombus and plaque, as outlined in previous paragraphs. Every reasonable attempt to keep blood pressure in an optimal range should be undertaken.

Given PTCA is performed under fluoroscopy, reaction to contrast agent may occur and can be a source of serious morbidity or even mortality in a small number of patients.[56, 57] A patient with a previous allergic reaction to contrast has an increased risk of a serious anaphylactic reaction. Patients with renal insufficiency are at risk for acute renal failure due to contrast. Patients with known cardiovascular disease who are taking

a beta-blocker are at increased risk for contrast reactions. Contrast agent reactions can be decreased by using non-ionic agents in those patients at high risk for adverse reactions, *e.g.*, diabetics or renal insufficiency. Also, observational studies have suggested that pre-treatment of a reaction-prone patient with a corticosteroid and/or an H1 and H2 histamine blocker can reduce this risk to an acceptable level when the indications for the procedure justify its need. Other methods of limiting contrast agent reactions are to properly hydrate the patient and minimize the volume of contrast agent.

Coagulopathy due to excessive heparinization is a known risk of interventional vascular procedures. Recently a number of adjunctive antithrombotic medications has been used for the purpose of reducing acute thrombus-related lesion site complications.[62] As these medications are powerful anticoagulants, a thorough understanding of their use and complications is necessary. Careful clinical and laboratory monitoring of the patient during the PTCA procedure will help minimize the occurrence of coagulopathies.

Coronary aneurysm formation after PTCA is a relatively uncommon complication, but the incidence is increasing due to the rise in complicated coronary interventions.[68, 69, 70] An iatrogenic coronary artery aneurysm forms when there is damage to the vessel wall during the procedure which results in aneurysmal dilatation. Use of techniques to limit vessel injury, such as careful advancement of guide wires and catheters will help to limit this complication.

Vascular access site complications consist primarily of hematoma, A-V fistula formation, pseudoaneurysm, and infection.[6, 11, 17, 46] Vascular access for PTCA is primarily through the femoral artery, with the brachial artery as an alternate route. Infection can be caused by inadequate aseptic technique or decreased host defenses. Strict attention to sterile technique during the procedure will help prevent most cases of wound infection at the vascular access site. Hematoma can be caused by use of excessive force or difficulty in placing the vascular access sheath, as can pseudoaneurysm. Hematoma can also result from inadequate pressure placed on the access site after the procedure due to technical difficulties or patient discomfort. Recently, the use of vascular sealing devices for closure of percutaneous arterial access sites has been reported.[66] Careful technique at the time of arterial access is needed to minimize the complication of an A-V fistula, which

may result from simultaneous puncture of an adjacent artery and vein. Percutaneous closure of femoral A-V fistulas has been reported using endovascular covered stents, as has open surgical repair.[71] The use of color doppler imaging should be considered for monitoring this type of complication.

Restenosis after successful PTCA has been reported to occur four to six months after the procedure in 25-30% of patients, and has been the single complication that most limits PTCA in clinical practice.[21, 23, 25, 72] While restenosis may be due to inadequate dilatation of the artery by PTCA, the process also commonly occurs in segments which have had optimal balloon dilatation. Restenosis, due to fibrocellular proliferation at the site of PTCA in the vessel wall, is a major factor why the use of stents in conjunction with angioplasty has become common practice.

Emergency bypass surgery can be due to failure of the angioplasty procedure, coronary dissection, or coronary occlusion. [5, 14, 22, 28, 32, 34, 42, 45] It has been recommended that surgical backup should be available for all angioplasties in case of complications during the procedure. Currently, the acceptable rate of emergency bypass surgery as a result of angioplasty is estimated to be < 2%.[62] The incidence of emergency bypass surgery can be decreased by attention to operative technique, and careful patient selection.

Death can be due to a wide variety of causes, some related to the procedure, and some related to the patient's underlying disease state.[3, 5, 8, 14, 20, 53, 54] Possible causes of mortality can be a massive MI, bleeding complications, failed procedure, or emergency bypass surgery. It may be difficult in some cases to determine if a death is procedure-related, especially in the case of a high-risk patient having an angioplasty for an acute indication such as unstable angina or a myocardial infarction. In contemporary practice, the expected death rate for PTCA should be < 1%.[62] Despite the fact that interventional cardiologists are attempting percutaneous revascularization procedures in patients with increasing clinical and angiographic complexity, the overall complication and mortality rates have remained unchanged or decreased over time.[67]

In addition to these clinical complications, there are potential device specific risks. Balloon rupture may occur due to inflating the balloon higher than the rated burst pressure, using a defective balloon, tissue calcification, or using an inappropriate balloon

inflation medium.[5] Results of balloon rupture range from no harm to the patient to severe complications related to vessel perforation, dissection, or rupture. To minimize this risk, the balloon should not be inflated greater than the rated burst pressure, and the use of a pressure monitoring device is recommended to prevent over-pressurization.

Another device specific risk that has been reported, although rarely, is guide wire entrapment and fracture.[26, 58, 59] This event has been attributed to excessive bending in a tortuous coronary vessel. The physician should be aware of this possibility when intervening in a patient with complex anatomy.

The PTCA procedure may fail due to device problems or difficulties related to patient coronary vascular anatomy. Operator inexperience can also be a contributing factor, especially with complex or difficult anatomy.[9, 19, 29, 40, 41] It may not be possible to cross the lesion with the balloon catheter, or once accessed, the lesion may be refractory to balloon dilatations within the recommended pressure guidelines. Current practice shows that angiographic success (at least one lesion successfully dilated by > 20%, with a residual stenosis of < 50%) occurs in nearly 90% of patients.[62] Ways to decrease the incidence of failed procedures are to select the patient carefully, and follow the manufacturers directions when using the balloon catheter. Inexperienced operators should have an experienced cardiologist standing by in case of more complex lesions.

In summary, the potential and reported risks associated with PTCA balloon catheters are well known and have been extensively documented over the last twenty years, in the literature as well as in PMA summaries of safety and effectiveness. Although these potential risks are numerous, they are well understood and may be minimized under the use of cardiologists experienced in interventional techniques, by using careful catheter technique, and by responsive patient monitoring. The numerous scientific articles which exist describing clinical experience with this type of device support its suitability for the intended use. Reasonable assurance of safe and effective use of these devices is demonstrated through extensive clinical experience with the device, the reported complication rates, and the well-documented instructional information which is available regarding the known potential complications associated with device use and how to minimize them. This information may be incorporated in device labeling guidance,

serving as a special control to support reasonable assurance of safety and effectiveness, allowing classification of PTCA balloon catheters into Class II.

## VII. MDR EXPERIENCE

Since enactment of the MDR regulations in December of 1984 and implementation of MAUDE in 1996, a total of 7449 reportable events are on record pertaining to the product classification code "74LOX" for percutaneous transluminal coronary angioplasty balloon catheters. Of these 7449 reports, 6503 are described in the MDR database (from January 1985 to December 1996) and 946 in the MAUDE database (from December 1996 to March 1999). The report types consist of malfunction (5822), injury (1439), death (111), and not specified (77). Please refer to the following table designating the incidence of the type of complication from each database.

**Table II: MDR/MAUDE DATA**

| Report Type | MDR (n=6503) | MAUDE (n=946) | Total Records (n=7449) |
|---|---|---|---|
| Malfunction | 5192 (79.8%) | 630 (66.6%) | 5822 (78.2%) |
| Injury | 1215 (18.7%) | 224 (23.7%) | 1439 (19.3%) |
| Death | 96 (1.5%) | 15 (1.6%) | 111 (1.5%) |
| Not Specified | ... | 77 (8.1%) | 77 (1.0%) |

As noted in Table II above, the types of complications reported over the last 15 years show the incidence of device malfunction to be decreasing (approximately 80% from 1985 to 1996, and 67% from 1996 to 1999). The incidence of injury and death are similar, with death comprising less than 2% of the reports, consistent with the incidence expected for patients undergoing PTCA (and in many cases with combinational treatment such as stent placement). The MDR and MAUDE events on record associated with the use of PTCA balloon catheters are among those that have been well documented and described in the published clinical reports pertaining to use of the various types of PTCA

balloons, as previously discussed in this submission. With the wealth of published information available coinciding with information reported by users and manufacturers, it is apparent that the use of this type of device is well understood and documented. This material supports the premise that sufficient information is available to provide reasonable assurance of the safe and effective use of PTCA balloon catheter devices through Class II controls.

## VIII. BIBLIOGRAPHY OF PUBLISHED LITERATURE

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